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IN VIVO EFFECTS OF OXYGEN AT VARYING PRESSURES ON ERYTHROCYTES --ETC(U)

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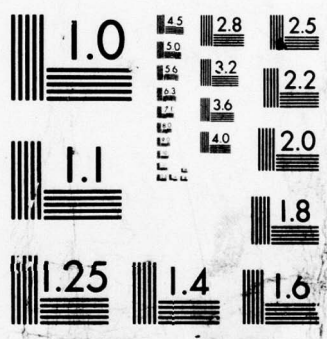
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OFFICE OF NAVAL RESEARCH

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In Vivo Effects of Oxygen at Varying
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The following is a list of the major scientific accomplishments achieved under support of this contract. Details of all of them are to be found in the publications derived from these studies.

1. First evidence of hemolysis in a human after exposure to oxygen under high pressure (OHP).
2. Evidence for a relationship between in vivo tocopherol status and central nervous system toxicity (seizures) during exposure to OHP.
3. Demonstration of in vivo inhibition of RBC cholinesterase by OHP and definition that it was due to peroxides.
4. First proof of in vivo peroxidation of lipid in RBCs (produced by hyperoxia).
5. Description of changes in RBC glycolytic intermediates due to OHP and associated enzyme changes.
6. Determination of the exact biochemical and functional events leading to in vivo destruction of RBCs by hyperoxia.
7. First evidence for in vivo consumption of tocopherol during exposure to hyperoxia.
8. Demonstration of in vivo changes in fatty acid composition of RBCs induced by hyperoxia and their relation to RBC destruction.
9. Evidence that hyperoxia of any degree could produce hemolysis if prolonged enough.
10. Demonstration of changes in WBCs produced by hyperoxia.
11. Effects of drugs on susceptibility of tissues (RBCs and brain) to hyperoxia.
12. Role of circadian rhythm in susceptibility to hyperoxic seizures.

13. Proof of in vivo production of H_2O_2 in RBCs and brain during exposure to hyperoxia.
14. Proof that senescent RBCs were those most susceptible to in vivo hyperoxia.
15. Study of factors that influence oxygen transport of RBCs.
16. Effect of drugs on red cells in humans that might influence susceptibility to hyperoxia.

PUBLICATIONS OF STUDIES DIRECTLY RELATED
TO THIS RESEARCH PROJECT

1. Mengel, C. E., Kann, H. E., Jr., Heyman, A., and Metz, E.: Effects of in vivo hyperoxia on erythrocytes. II. Hemolysis in a human after exposure to oxygen under high pressure. *Blood* 25:822-829, 1965.
2. Zirkle, L. G., Jr., Mengel, C. E., Horton, B. D., and Duffy, E. J.: Studies of oxygen toxicity in the central nervous system (CNS). *Aerospace Med.* 36:1027-1032, 1965.
3. Mengel, C. E., Zirkle, L. G., Jr., O'Malley, B. W., and Horton, B. D.: Studies of the mechanism of in vivo RBC damage by oxygen. *Aerospace Med.* 36:1036-1041, 1965.
4. Zirkle, L. G., Jr., Mengel, C. E., Butler, S. A., and Fuson, R.: Effects of in vivo hyperoxia on erythrocytes. IV. Studies in dogs exposed to hyperbaric oxygenation. *Proc. Soc. Exp. Biol. & Med.* 119:833-837, 1965.
5. O'Malley, B. W., Mengel, C. E., Meriwether, W. D., and Zirkle, L. G., Jr.: Inhibition of erythrocyte acetylcholinesterase by peroxides. *Biochem.* 5:40-44, 1966.
6. Mengel, C. E., and Kann, H. E., Jr.: Effects of in vivo hyperoxia on erythrocytes. III. In vivo peroxidation of erythrocyte lipid. *J. Clin. Invest.* 45:1150-1158, 1966.
7. Kann, H. E., Jr., and Mengel, C. E.: Mechanisms of erythrocyte damage during in vivo hyperoxia. *Proc. 3rd Int. Conf. on Hyperbaric Medicine.* November, 1966, pp. 65-72.
8. O'Malley, B. W., and Mengel, C. E.: Effects of in vivo hyperoxia on erythrocytes. V. Changes of RBC glycolytic intermediates in mice after in vivo oxygen under high pressure. *Blood* 29:196-202, 1967.
9. Kann, H. E., Jr., Mengel, C. E., Clancy, W. T., Timms, R. M.: Effects of in vivo hyperoxia on erythrocytes. VI. Hemolysis occurring after exposure to oxygen under high pressure (OHP). *J. Lab. & Clin. Med.* 70:150-157, 1967.
10. Mengel, C. E., Kann, H. E., Jr., and Timms, R. M.: Transient and differing effects of in vivo hyperoxia on erythrocytes. *Proc. 3rd Ann. Conf. on Atmospheric Contamination in Confined Spaces.*

11. Timms, R. M., and Mengel, C. E.: Effects of in vivo hyperoxia on erythrocytes. VII. Inhibition of RBC phosphofructokinase. *Aerospace Med.* 39:71-73, 1968.
12. Szabo, S. J., and Mengel, C. E.: Effect of diet and in vivo hyperoxia on plasma tocopherol levels. *Amer. J. Med. Sci.* 255:132-136, 1968.
13. Smith, D., Timms, R. M., Mengel, C. E., and Jefferson, D.: Effects of in vivo hyperoxia on erythrocytes. VIII. Effect of adenosine triphosphate (ATP) and related glycolytic enzymes. *Johns Hopkins Med. J.* 122:168-171, 1968.
14. Mengel, C. E.: Rancidity and the red cell. *Amer. J. Med. Sci.* 255:341-347, 1968.
15. Carolla, R. L., Mengel, C. E., and Husney, R. M.: Effect of in vivo hyperoxia on erythrocyte and fatty acid composition. *Aerospace Med.* 38:1290, 1968.
16. Goldstein, J. R., Mengel, C. E.: Hemolysis in mice exposed to varying levels of hyperoxia. *Aerospace Med.* 40:12-13, 1969.
17. Goldstein, J. R., Mengel, C. E., Carolla, R. L., and Ebbert, L.: The relationship between tocopherol status and in vivo hemolysis caused by hyperoxia. *Aerospace Med.* 40:132-135, 1969.
18. Osborne, C. K., Brubaker, L. H., and Mengel, C. E.: Effects of hyperoxia on white blood cells. *Aerospace Med.* 41:1176, 1970.
19. Serrill, W. S., Jefferson, D., Quick, J., and Mengel, C. E.: Effect of acetylsalicylic acid and ascorbic acid on oxygen toxicity. *Aerospace Med.* 4:156-164, 1971.
20. Johnson, W., Jefferson, D., and Mengel, C. E.: In vivo hemolysis due to hyperoxia: Role of H_2O_2 accumulation. *Aerospace Med.* 43:943-945, 1972.
21. Serrill, W. S., Jefferson, D., and Mengel, C. E.: Effects of hyperoxia and tocopherol deficiency on nitrite-induced methemoglobinemia. *Aerospace Med.* 42:1293, 1971.
22. Hof, D. G., Dexter, J. D., and Mengel, C. E.: Circadian variations in oxygen toxicity seizures. *Aerospace Med.* 42:1293, 1971.
23. Mengel, C. E.: The red cell and hyperoxia. *Physiological Pharmacology*, Vol. 5, 1974.
24. Mengel, C. E.: The effects of hyperoxia on red cells as related to tocopherol deficiency. *Ann. N.Y. Acad. Sci.* 203:163-171, 1972.
25. Johnson, W., Jefferson, D., and Mengel, C. E.: In vivo formation of hydrogen peroxide in red cells during exposure to hyperoxia. *J. Clin. Invest.* 51:2211-2213, 1972.

26. Osborne, C. K., Carolla, R. L., Jefferson, D., and Mengel, C. E.: Effect of methemoglobin on in vivo RBC lipid peroxidation. *Aerospace Med.* 44:63-67, 1973.
27. Jerrett, S., and Mengel, C. E.: Seizures, H_2O_2 and lipid peroxides in brain during exposure to oxygen under high pressure. *Aerospace Med.* 44:40-44, 1973.
28. Hof, D. G., Dexter, J. D., Cline, W. J., Jr., and Mengel, C. E.: CNS epinephrine tone, a possible etiology for the threshold in susceptibility to oxygen toxicity seizures. *Aerospace Med.* 43:1194-1199, 1972.
29. Dexter, J. D., Hof, D. G., and Mengel, C. E.: The effect of sleep-wake reversal on the circadian rhythm of oxygen toxicity seizure susceptibility. *Aerospace Med.* 43:1075-1078, 1972.
30. Carolla, R. L., Brubaker, L. H., and Mengel, C. E.: Age of red cells destroyed by hyperoxia. *Aerospace Med.* 45:1273-1275, 1974.
31. Hirszel, P., Maher, J. F., Tempel, G. E., and Mengel, C. E.: Effect of hemodialysis on factors influencing oxygen transport. *J. Lab. & Clin. Med.* 85:978, 1975.
32. Nolph, K. D., Montie, J., and Mengel, C. E.: Treatment of end stage kidney disease. *Missouri Medicine*, Vol. 72, 4:175, 1975.
33. Kimzey, S., Fischer, C., Johnson, P., Ritzman, S., and Mengel, C. E.: Hematology and immunology studies: Biomedical results of Apollo. NASA Pub., Washington, D. C., 1975.
34. Mengel, C. E. and Greene, H. L.: Effects of ascorbic acid on red blood cells. *Ann. Int. Med.* 84:490, 1976.

PUBLICATIONS OF STUDIES INDIRECTLY RELATED
TO THIS RESEARCH PROJECT

1. Mengel, C. E., Kann, H. E., and O'Malley, B. W.: Increased hemolysis after intramuscular iron administration in patients with paroxysmal nocturnal hemoglobinuria. Report of six occurrences in four patients, and speculations on a possible mechanism. *Blood* 26:74-81, 1965.
2. Mengel, C. E.: Hemolytic anemia in Current Therapy, Saunders Co., pp. 190-191, 1966.
3. Meriwether, W. D., and Mengel, C. E.: Peroxidation of lipid from normal and paroxysmal nocturnal hemoglobinuria erythrocytes. *Nature* 210:91, 1966.
4. Mengel, C. E., Metz, E., and Yancey, W. S.: Anemia during acute infections. Role of glucose-6-phosphate dehydrogenase deficiency in Negroes. *Arch. Int. Med.* 119:287-290, 1967.
5. Mengel, C. E., and Klavins, J. V.: Development of hemolytic anemia in rats fed methionine. *J. Nutrition* 92:104-110, 1967.
6. Kann, H. E., Jr., Mengel, C. E., and Wall, R. L.: Paroxysmal nocturnal hemoglobinuria obscured by the presence of iron deficiency. *Ann. Int. Med.* 67:593-596, 1967.
7. Mengel, C. E., Kann, H. E., Jr., and Meriwether, W. D.: Studies of paroxysmal nocturnal hemoglobinuria erythrocytes: Increased lysis and lipid peroxide formation by hydrogen peroxide. *J. Clin. Invest.* 46:1715-1723, 1967.
8. Meriwether, W. D., and Mengel, C. E.: Peroxidation of lipid from paroxysmal nocturnal hemoglobinuria-like erythrocytes. *Nature* 216:85-86, 1967.
9. Meriwether, W. D., Mengel, C. E., and Kann, H. E., Jr.: Effect of reduced glutathione on erythrocyte lipid. *Proc. Soc. Exp. Biol. Med.* 127:60, 1968.
10. Kann, H. E., Jr., Mengel, C. E., Meriwether, W. D., and Ebbert, L.: Production of in vitro lytic characteristics of paroxysmal nocturnal hemoglobinuria erythrocytes in normal erythrocytes. *Blood* 32:49-58, 1968.

11. Smith, K. A., and Mengel, C. E.: The association of iron-dextran induced hemolysis and lipid peroxidation in mice. *J. Lab. & Clin. Med.* 72:505-510, 1968.
12. Baum, N. H., Mengel, C. E., and Balcerzak, S. P.: Effect of reduced glutathione on rat erythrocytes: Production of PNH-like (paroxysmal nocturnal hemoglobinuria) features. *J. Lab. & Clin. Med.* 73:277-282, 1969.
13. Graff, K. S., Mengel, C. E., and Balcerzak, S. P.: Inhibition of in vitro PNH erythrocytes lysis by tryptophan metabolites. *J. Lab. & Clin. Med.* 73:399-404, 1969.
14. Bowman, M., Ottolenghi, A. C., and Mengel, C. E.: Effects of phospholipase C on human erythrocytes. *J. Membrane Biology* 42:436-438, 1971.
15. Mengel, C. E., Ebbert, L., Stickney, D., Brubaker, L. H., and Essig, L.: The biochemistry of the PNH red cell. *Series Hematologica*, Vol. V, 3, 88-100, 1972.
16. Brubaker, L. H., Schaberg, D. A., Jefferson, D., and Mengel, C. E.: A potential rapid screening test for paroxysmal nocturnal hemoglobinuria. *New Eng. J. Med.* 288:1059-1060, 1973.
17. Mengel, C. E.: The problem of drug induced anemia. *Journal of Continuing Education* 1:26, 1973.